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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

KIM, TAEYOON

ART UNIT

PAPER NUMBER

1651

NOTIFICATION DATE

DELIVERY MODE

01/27/2009

ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

pat-dept@quarles.com

<b>Office Action Summary</b>	<b>Application No.</b> 10/717,677	<b>Applicant(s)</b> PALECEK ET AL.	
	<b>Examiner</b> TAEYOON KIM	<b>Art Unit</b> 1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 12 November 2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1,4-13 and 16-28 is/are pending in the application.
- 4a) Of the above claim(s) 1,4-12 and 25 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 13,16-24,26 and 27 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

Claims 1, 4-13 and 16-28 are pending.

#### ***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/12/2008 has been entered.

Applicant's amendment and response filed on 11/12/2008 has been received and entered into the case.

Claims 2, 3, 14 and 15 have been canceled, claims 1, 4-12 and 25 have been withdrawn from consideration as being drawn to non-elected subject matter, and claims 13, 16-24, 26 and 27 have been considered on the merits. All arguments have been fully considered.

Applicant's arguments with respect to claims 13, 16-24, 26 and 27 based on Reubinooff et al. under 35 U.S.C. §102 have been considered but are moot in view of the new ground(s) of rejection.

It is noted that in the previous office action mailed on 9/27/2007, the examiner dealt with the limitations in regard to the culture composition comprising hES undifferentiated cells, unconditioned media, a flexible solid porous matrix, and an apparatus capable of applying periodic strain on the matrix and the cells (see p. 3-9).

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However, the claim rejection has been withdrawn due to the amendment upon the subsequent OA mailed on 7/8/2008. Upon the current amendment, it is necessary to reinstate the claim rejection, and the response filed on 3/25/2008 is re-considered along with the response filed on 11/12/2008.

In the response filed on 3/25/2008 to the office action mailed on 9/27/2007, applicant argued that a skilled person interested in maintaining proliferating human ES cells would not place the cells in an apparatus for promoting differentiation (p.8 of the response). The examiner respectfully disagrees with this assertion.

The claims are drawn to the product, and any process step which does not provide any structural limitation to the product would not limit the product claims. The current claims do not particularly disclose a positive process step. However, it implies that a process step of applying a periodic strain using the apparatus on undifferentiated hES cells would result in more proliferation. This implication would not provide any structural limitation to the product, particularly such a process step is not required for the current claims. The current claims require undifferentiated hES cells, flexible porous matrix (i.e. Matrigel), BioFlex plate, unconditioned culture medium, and an apparatus capable of applying periodic strain, and the teaching of Russell et al. in view of Xu et al. satisfies these limitations, and thus renders them obvious.

Applicant argument that a person of ordinary skill in the art would not use the apparatus for proliferation since the apparatus is being used for differentiation. Whether or not the intended purpose of the apparatus being differentiation or proliferation of cells, the intended use of the apparatus does not limit the product.

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Furthermore, It is understood that the effect/result of such a mechanical strain by the apparatus is dependent on the property of the cells being utilized, rather than the apparatus per se. It is the cells' intrinsic property to react to the mechanical strain, and the outcome of mechanical strain would be based on the cell rather than the apparatus. Since Russell et al. in view Xu et al. teach the same undifferentiated hES cells, the outcome (intended results) would be the same as the claimed invention.

Whether or not the undifferentiated hES cells being resulted in proliferation from the periodic strain or other method (e.g. simply add more of undifferentiated hES cells to the culture composition), the process step does not limit for the composition claims unless providing structural limitation to the product, and the culturing method using the apparatus would not change the nature or property or structure of undifferentiated hES, or those other components of the composition. Therefore, even if the implied method step of periodic strain is considered in the claims, the method steps do not provide any structural differences into the cells, matrix (Matrigel) and the apparatus. Therefore, the teachings of Russell et al. in view of Xu et al. render the claims obvious.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

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the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 13, 16-24, 26 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Russell et al. (of the record) in view of Xu et al. (of the record).

Russell et al. teach a hES cell culture composition (see paragraph [0106]) grown on hydrogel matrix (see paragraph [0015]), and an apparatus [Flexercell strain system (FX-3000) and BioFlex plate] (see paragraph [0161]) on which the cells are stretched by a vacuum (see paragraph [0146]). Russell et al. also teach the percentage of strain starting at 5% (see paragraph [0179]) and the frequency of strain or pattern of strain can be readily varied by programming the system (see paragraph [0146]).

Russell et al. do not teach the human embryonic stem cells being grown on Matrigel (flexible porous matrix).

Xu et al. teach a culture of human embryonic stem (hES) cells on Matrigel without fibroblast feeder cells (see Abstract and Fig. 1). Xu et al. also teach undifferentiated hES cells on Matrigel in non-conditioned ES medium (see Fig. 1J). Xu et al. also teach the undifferentiated hES cells are positive for surface markers such as Oct4 and SSEA-4, and also positive for alkaline phosphatase (see Fig.1 and p.972, left column, 2<sup>nd</sup> paragraph).

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It would therefore have been obvious for the person of ordinary skill in the art at the time the invention was made to substitute the hydrogel taught by Russell et al. with Matrigel taught by Xu et al. because a person of ordinary skill in the art would recognize Matrigel would be an art-recognized equivalent matrix to the hydrogel for cell culture.

M.P.E.P. §2144.06 states “In re Scott, 323 F.2d 1016, 139 USPQ 297 (CCPA 1963) (Claims were drawn to a hollow fiberglass shaft for archery and a process for the production thereof where the shaft differed from the prior art in the use of a paper tube as the core of the shaft as compared with the light wood or hardened foamed resin core of the prior art. The Board found the claimed invention would have been obvious, reasoning that the prior art foam core is the functional and mechanical equivalent of the claimed paper core. The court reversed, holding that components which are functionally or mechanically equivalent are not necessarily obvious in view of one another, and in this case, the use of a light wood or hardened foam resin core does not fairly suggest the use of a paper core.); Smith v. Hayashi, 209 USPQ 754 (Bd. of Pat. Inter. 1980) (The mere fact that phthalocyanine and selenium function as equivalent photoconductors in the claimed environment was not sufficient to establish that one would have been obvious over the other. However, there was evidence that both phthalocyanine and selenium were known photoconductors in the art of electrophotography. “This, in our view, presents strong evidence of obviousness in substituting one for the other in an electrophotographic environment as a photoconductor.” 209 USPQ at 759.).”

With regards to the limitations of “wherein more of the human ES cells ... not

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configured to apply periodic strain to the matrix and the human ES cells.” in the claims, it is considered that the limitation does not provide any structural limitation to the claimed invention difference in comparison to the product disclosed by the references. Rather, the limitation merely states the result of the limitations drawn to the method step of applying such periodic strain and therefore, adds nothing to the patentability or substance of the claim. Therefore, this phrase does not limit the claim. See *Texas Instruments Inc. v. International Trade Commission*, 26 USPQ2d 1010 (Fed. Cir. 1993); *Griffin v. Bertina*, 62 USPQ2d 1431 (Fed. Cir. 2002); *Amazon.com Inc. v. Barnesandnoble.com Inc.*, 57 USPQ2d 1747 (Fed. Cir. 2001).

With regard to the limitations drawn to the apparatus of the claims being configured to apply mechanical strain, vacuum pressure, or oscillatory stretching to the matrix and the hES cells, or to exert at least about 5% on the matrix or to stretch at least about 6 times per minutes, the apparatus of Russell et al., Flexercell system, is identical to the claimed apparatus and therefore, the apparatus can be configured to carry out the claimed limitations and thus, it renders the claims obvious.

Furthermore, it would have been obvious for a person of ordinary skill in the art because Russell et al. clearly indicates that varying patterns of strain (e.g. sinusoidal, stepwise, sustained, etc) can be readily programmed using factory-installed protocols using Flexercell strain unit (see paragraph [0146]), thus the various strain rate or the mode of stretching used in the claimed invention are result effective variables and effectively modified by programming the unit. As such, the variables would be routinely optimized by one of ordinary skill in the art in practicing the invention disclosed by those



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references. Generally, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); >see also *Peterson*, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."); \*\* *In re Hoeschele*, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969) (Claimed elastomeric polyurethanes which fell within the broad scope of the :references were held to be unpatentable thereover because, among other reasons, there was no evidence of the criticality of the claimed ranges of molecular weight or molar proportions.). For more recent cases applying this principle, see *Merck & Co. Inc. v. Biocraft Laboratories Inc.*, 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989); *In re Kulling*, 897 F.2d 1147, 14 USPQ2d 1056 (Fed. Cir. 1990); and *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997). Accordingly, the claimed invention was prima facie obvious to one of ordinary skill in the art at the time the invention was made especially in the absence of evidence to the contrary.

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Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill at the time the invention was made.

***Conclusion***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TAEYOON KIM whose telephone number is (571)272-9041. The examiner can normally be reached on 8:00 am - 4:00 pm ET (Mon-Thu).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Taeyoon Kim/  
Examiner, Art Unit 1651